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09/852,547	05/10/2001	David A. Sirbasku	1944-00800	6474

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/852,547	Sirbasku	
	Examiner	Art Unit	
	Karen A. Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-8,12-15,17-20,66-69,71,73-79 and 81-94 is/are pending in the application.

4a) Of the above claim(s) 90 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-8,12-15,17-20,66-69,71,73-79,81-89 and 91-94 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/27/2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 2, 3, 5, 7, 8, 12, 13, 14, 15, 17, 18, 19, 20, 66, 67, 68, 69, 71, 73, 74, 75, 76, 77, 78, 82, 83, 84, 85, 86 and 89 have been amended. Claims 9-11, 70, 72 and 80 have been canceled. Claims 91-94 have been added. Claims 1-8, 12-15, 17-20, 66-69, 71, 73-79, 81-94 are pending. Claim 90, drawn to a non-elected invention, is withdrawn from consideration. Claims 1-8, 12-15, 17-20, 66-69, 71, 73-79, 81-89 and 91-94 are under consideration.

2. Claim 91 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 67. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

3. The rejection of claims 1-6, 12, 17-19, 66, 67, 70, 73-76 and 81-86 and 89 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons of record. New claim 94 is also rejected for the reasons of record below. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

Claims 1-6, 12, claim 17 in part, 18 in part, 19 in part, 66, 67, 70, 73-76 and 81-86, 89 and 91 are rejected under 112, first lack of enablement for quantitating or detecting an immunoglobulin inhibitor of steroid hormone responsive cell growth in a specimen of body fluid or secretion. the specification states on page 10, [0018] that for "purpose of this disclosure, the term "immunoglobulin inhibitor" refers to a secretory immunoglobulin, preferably on of the secretory immunoglobulins IgA, IgM and Ig1 that is active for inhibiting proliferation of a steroid hormone responsive cancer cell. The specification bases the instant claims on the premise that measurement of said secretory immunoglobulins would then be diagnostic for inhibition of steroid responsive cell growth and that decreased levels of said immunoglobulins would then be indicative of decreased inhibition of said cell growth. The specification teaches that the secretory immunoglobulin system decreases activity with age. This is a general teaching

dependent upon the averaging of multiple measurements of secretory immunoglobulins over a period of time encompassing years. However, it is known in the art that levels of IgA, the major secretory immunoglobulin, vary as a function of time of day, as well as within a year, and large variations between healthy subjects is documented (Garde et al, Clinical Chemistry, 2000, Vol. 46, pp. 551-559, cited in a previous action). The art also teaches that levels of secretory IgA is hormonally regulated in women and thus variable over the curse of a menstrual cycle (Gomez et al, Amer J Reproduc Immunol, 1993, Vol. 29, pp. 219-223, cited in a previous action). It would be reasonable to conclude that the level of the other types of secretory immunoglobulins would also vary as a function of the exposure of an individual to exogenous antigens or substances provoking an immune reaction. Thus, it would be reasonable to conclude that the measurement of secretory immunoglobulins in a single sample would not be representative of the average level of secretory immunoglobulins present within an individual during the course of a year or more. Given that the art teaches that the level of IgA, the major secretory immunoglobulin, varies both positively and negatively with time in a healthy individual and also varies between individual subjects and thus supports the conclusion that the level of other secretory immunoglobulins also vary with time by both increasing and decreasing; and given the lack of teachings in the specification regarding ranges or levels of secretory immunoglobulins that were indicative of normal individual versus individuals having a steroid hormone responsive cancer, one of skill in the art would be subject to undue experimentation in order to make and use the claimed methods relying on correlating the levels of secretory immunoglobulins with the presence or susceptibility to steroid hormone responsive cancer. Further, Sullivan et al (Immunology, 1983, Vol. 49, pp. 379-386) observe that the transudation of IgA in the uterus is mediated through the hormonal control of secretory component (page 380, first column, lines 23-29), but that the estrodiol accumulation of secretory component appears to be independent of IgA, because of the demonstration that dexamethasone suppressed IgA accumulation but not secretory protein accumulation (page 379, first column, lines 14-18). Notably, Sullivan et al state that following estradiol treatment, the source of uterine IgG appears to be plasma.

Hurlimann et al (Virchows Arch A Path Anat and Histol, 1978, Vol. 377, pp. 211-223) observe that in human biopsies of the endometrium that the endometrium did not synthesize immunoglobulins; secretory component was synthesized only by endometrial tissue in the

secretory phase and by some carcinomas (Summary, lines 13-16). Hurlimann et al observe that there is no relationship between the production of secretory component and the presence of IgA plasmacytes which localize as a result of immunologic influences within the tissues studied (summary, lines 16-19). Hurlimann et al disclose that in cervical tissues without a pathologic lesion exhibited few plasmacytes around glands and under the surface epithelium, and that culturing of the samples in vitro led to the identification of a very low level of synthesized immunoglobulins within the tissue (page 213, under the heading "Cervical Tissues without Lesion"). Hurlimann et al disclose that a low level of immunoglobulin synthesis could be detected by the culturing of neoplastic cervical tissue and that said tissue also showed few plasmacytes (page 214, under the heading of "Cervical Tissues with Metasplasia", in contrast to cervical neoplasia where the synthesis of IgG and IgA was marked and correlated with the presence of numerous IgG and IgA plasmacytes (page 215-216, under the heading "Carcinoma in Situ"). Hurlimann et al disclose that in the culturing of endometrial carcinoma biopsy samples the numerous IgG plasmacytes demonstrated immunoglobulin synthesis (page 219, under the heading of "Carcinoma"). Hurlimann et al conclude that secretory component is synthesized in excess when compared to the synthesis of IgA (page 219, lines 18-21 under the heading "Discussion"). Hurlimann et al disclose that although IgA synthesis in the samples examined is decreased in the age group between 44-68 years, loss of IgA synthesis is replaced by IgG synthesis (page 219, lines 27-35, under the heading of "Discussion"). Thus, it can be concluded that the transcytosis of secretory immunoglobulin is dependent upon the presence of local plasmacytes or the presence of an immunoglobulin in the serum. Further, Fudenberg et al (Basic and Clinical Immunology, 1978, page 326, pp. 324-328) teach that overall serum concentrations of IgG and IgA tend to increase with age whereas serum IgM tends to decrease (especially, page 326, second column, lines 9-10). Therefore, one of skill in the art would not conclude that persons of advancing age were deficient in IgG or IgA in serum levels, or IgG in mucosal levels.

Richarson et al (Journal of Steroid Biochemistry and Molecular Biology, 1993, Vol. 47, pp. 143-149) disclose that Il-6 and IFN-gamma in conjunction with estrogen resulted in an increase of both secretory component and IgA levels in uterine secretions in rat uteri and concluded that the regulation of secretory component is complex because it is controlled by the interactions of cytokines and sex hormones through both autocrine and paracrine effects (page

132, second column, lines 12-22). Brandtzaeg et al (In: Developments in Biological Standarization, Brown and Haaheim, Ed.s, March 1998, Vol. 92, pp. 93-108) teach that secretory component can be up-regulated by IFN-gamma, Il-4 and TNF-alpha (pages 95-96, bridging sentence) which corroborates the teachings of Richardson et al. Verrijdt et al (Biochem Soc Transactions, 1997 May, Vol. 25, page 186S) report that human secretory component gene expression is under the influence of TNF-alpha, IFN-gamma, TGF-beta, glucocorticoids, estrogens and androgens, but the influence of estrogen appears to be opposed in the mammary gland and in the uterus (column 1, first paragraph). It is noted that the instant claims are broadly drawn to encompass any type of epithelial cancer, not just breast, and any type of steroid hormone response, not just a response to estrogen, and that the response to estrogen is a function of the tissue type.

Tamiolakis et al (European Journal of Gynaecological Oncology, 2002, Vol. 23, pp. 453-456) discloses that the expression of secretory component increases as endometrial hyperplasia progresses to endometrial carcinoma (page 455, second column, last sentence). One of skill in the art would reasonably conclude that the transurdation of immunoglobulins would be increased as a result of the progression to cancer, because there is more secretory component available to transcytosis any available immunoglobulin.

Klein et al (Journal of the National Cancer Institute, 1978, Vol. 61, pp. 57-60) teaches that the level of free secretory component increased dramatically in mucinous cyst fluid and ovarian carcinomas and in particularly mucinous adenocarcinomas (page 58, first two paragraphs under the heading of "results"). One of skill in the art would reasonably conclude that the transurdation of immunoglobulins by these tissues would be increased because there is more secretory component available to transcytosis any available immunoglobulin. Garcia et al (American Journal of Obstetrics and Gynecology, 1977, Vol. 129, pp. 281-284) report that effusions from 12 epithelial tumor of the ovary comprises IgG, IgM and IgA, whereas in non-cancerous ovarian tissue, only IgG was detected (abstract, lines 1-6). One of skill in the art would reasonably conclude that the tumors were associated with IgM as well as IgA. Garcia et al teach that free secretory component was detected in all malignant and benign samples, therefore the tumor had not lost the ability to transcytose immunoglobulins.

Thalman et al (American Journal of Obstetrics and Gynecology, 1979, Vol. 134, pp. 899-903) teach that increased secretory component is detected in the plasma of patients with tumors of the colon, lung, breast, bladder and ovary (page 899, column 1, lines 9-11). It can be reasonably concluded that the tumor is the source of the increase in free secretory component, therefore said tumor would be able to transcytose immunoglobulins from serum or local plasmacytes.

Given the above teaching of the prior art, one of skill would reasonably conclude that in or around epithelial tumors the local levels of immunoglobulins are increased or at the same level as in normal tissue. One of skill in the art would also conclude that secretory component is up-regulated in tumors relative to normal tissues and that the increase in secretory component associated with tumorigenesis would imply an increase transcytosis of available immunoglobulins. It would also be reasonably concluded in light of the teachings of Tamiolakis et al that pre-neoplastic cells would exhibit and intermediate level of secretory component expression and therefore would exhibit an intermediate level of transcytosis. Further, the teachings of Hurlimaan and Fudenberg do not support an overall decrease in immunoglobulins available for transcytosis by the secretory component. One of skill in the art would not be able to use the instant methods because they are contrary to the observations in the art, that levels of immunoglobulins in the vicinity of epithelial tumors do not decline, and in some cases are increased relative to normal tissue.

4. Applicant argues that the specification is fully enabling for the instant claims because methods for carrying out the required measurements are well known in the art. This has been considered but not found persuasive, as there would be no reasonable expectation of success that the presence of neoplastic tissue which had the potential to develop into a cancer would be evident from a decrease in immunoglobulin levels for the reasons set forth above, i.e., that the expectation would be that no change in immunoglobulin levels would be evident, or that immunoglobulin levels would parallel secretory component levels and increase in a tissue progressing to a cancerous state. Applicant argues that the levels of inhibitory immunoglobulins assess by the disclosed measurement of inhibition in culture have a nexus with the levels of immunoglobulins found in vivo. This has been considered but not found persuasive. The art

teaches that plasmacytes and serum carry the immunoglobulins to the basolateral side of epithelial cells and the secretory immunoglobulin system is responsible for transcytosis of said immunoglobulins to the apical portion of the epithelial cell where they are cleaved from the cell by proteases and thereby delivered to mucosal excretions. The art teaches that the secretory component is synthesize in excess of the immunoglobulin transcytosis. Thus, the level of secretory immunoglobulins would be determined by the overall level of immunoglobulins available for transcytosis, and for the reasons set forth in the above enablement rejection, have no nexus with the progression to cancer.

5. Claims 7, 8, 13, 14, 17, 19, 20, 67, 68, 69, 77-79, 88, 91, 92 and 93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(A) As drawn to inadequate description of a genus

Claims 8, 9, 10, 11, 13, 14, 17, 19, 67, 72, 80 and 88 contain the limitations of "mediator of immunoglobulin inhibition of steroid hormone responsive cell growth". "defective mediator of immunoglobulin inhibition of steroid hormone responsive cell growth", "a poly-Ig receptor" "an Fc receptor" , a "variant Fcgamma receptor", and "altered domain in said poly Ig receptor". The specification states on page 11[0022] that "certain other embodiments of the invention provide a method of detecting a mediator of immunoglobulin inhibition of steroid hormone responsive cell growth that includes detecting a poly-Ig receptor". Thus, claims drawn to an immunoglobulin inhibitor of cell growth comprises a genus of inhibitors which include a poly-Ig receptor but is not limited only to poly-Ig receptors. further, given that the claim limitations require the determination of mediation of inhibition of steroid hormone cell growth , it in concluded that claims drawn to poly-Ig receptors and Fc receptors encompass defective and variant receptors which differ in amino acid sequence and function from the wild type receptors.

The instant method claims rely on the identity of variant poly-Ig, variant Fcgamma receptors, variant TGF-beta and genes. The claims are thus drawn to a genus of molecules encompassing mutant, truncated and otherwise variant poly-Ig, Fc receptor proteins and TGF-

beta. The claims do not limit the "defect" in terms of specific structural or specific functional characteristics., thus it is not possible to determine if a given protein is member of the claimed genus The specification does not teach a representative number of defective poly-Ig receptors or defective Fc receptors that would be representative of the claimed genus. Because the genuses are highly variant, reliance on a description of the wild-type poly-Ig receptor or the Fcgamma receptor or the wild-type TGF-beta is insufficient to anticipate the claimed genus. The specification provides no teachings regarding DNA sequence or the protein encoded therefrom for any of the aforesaid variants or alleles of the poly Ig receptor or the Fc receptor. Claims 20, 77-79 and 93 are method claims relying on the identity of an "estrogen binding activity having a greater E2 binding affinity than that of ERalpha or ERbeta. The specification does not provide any structural information about said activity, and therefore lacks written description of said "activity".

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists

of, is not a description of that material." Id. Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product. Thus, the instant specification may provide an adequate written description of variants, per Lilly by structurally describing a representative number of variants which negatively influence the inhibition of steroid hormone responsive cell growth or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus.". Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the steroid hormone/steroid hormone receptor, the defective poly-Ig receptor, the defective Fc receptors or the alternative alleles of the poly-Ig receptors, Fc receptor or TGF-beta to practice the methods of the instant invention in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete or partial structure or physical or chemical structure of the variants or alleles, nor any

physical or chemical characteristics coupled with a known or disclosed correlation between structure and function. Regarding alleles and defective gene sequences, the specification does not identify said variant gene sequences. The general knowledge and skill in the art concerning alleles is that the structure of one allele is not representative of other unknown alleles. The same can be said of mutant genes, such as those encoding "defective" poly Ig receptor and defective Fc receptors. thus, the nature of both alleles and defective Fc receptors and defective poly Ig receptors is that they are variant structures and the in the present state of the art, the structure of one does not provide guidance for the structure of other s. The common attributes of the genus are not described. Thus, it is concluded that the specification does not provide a description of the disclosed steroid hormone receptor, variant poly-Ig receptors, variant Fc-receptors of alleles of TGF-beta that would satisfy the standard set out in Enzo.

Thus, the specification does not provide an adequate written description of the defective poly Ig receptors, defective Fc receptors, steroid hormone receptors, alleles participating in the allelic imbalance of poly-Ig receptors, Fcgamma receptors or TGF-beta receptor, required for the practice of the instant method claims. Since the specification fails to adequately describe disclosed immunoglobulin inhibitor, "a" poly Ig receptor or "a" Fc receptor and steroid hormone/steroid hormone receptor, it also fails to adequately describe the method reliant upon said products.

(B) As drawn to new matter

Claims 17, 19, 20, 77-79, 86 and 93 are rejected for the incorporation of new matter. Claim 17 has been amended to incorporate the limitation "a deletion of one or more of said second set of conditions indicating early onset of said cancerous or precancerous lesions". Claim 19 has been amended to incorporate the limitation "the presence of one or more conditions from step (c) is further indicative of at least some degree of reduced prognosis". Claim 20 has been amended to recite the limitations "indicating an estrogen-based therapy" and "contra-indicating an estrogen based therapy fro treating said cancer". Claim 93 has incorporated the limitation "the ability of said poly-Ig receptor to bind to the Fc domain of dimeric/polymeric IgA or polymeric IgM further indicates a therapy for treating said cancer". The specification as filed lacks adequate written description for the amended claims. Applicant has not pointed out by

page and line number the location in the specification which provides support for this amendment.

6. Claims 8, 67, 68 and 91 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting a functional poly-Ig receptor, or a functional Fc receptor, does not reasonably provide enablement for a method for the method of detecting non-functional receptors of poly-Tg or Fc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims..

The instant claims are drawn to the detection of receptors mediating steroid hormone responsive cell growth, which is drawn to in part tot eh detection of functional receptors as well as non-functional receptors

The specification has identified the poly-Ig receptor as the epithelial receptor for IgA and IgM (example 24) and an "Fc-like" epithelial receptor for IgG1 (example 25). The specification has not provided any identity of mutated or otherwise defective poly-Ig receptors or Fc-like receptors. The specification has demonstrated that IgA, IgM or IgG1 can inhibit the growth of steroid dependent cancer cell lines in culture. The specification has not provided any evidence that this phenomenon would not be applicable to normal non-cancerous cells, or that cancer cells in culture or in vivo have defective poly-Ig receptors or Fc-like receptors which cannot mediate the observed inhibition. It is noted that all the cancer cells set forth in specific examples by the specification are inhibited by the immunoglobulins and therefore exhibit functional inhibition of steroid hormone responsive cell growth and therefore would not be expected to have defective or decreased poly-Ig or defective or decreased Fc-like receptors. Therefore one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to carry out the claimed methods with respect to the identification of defective poly-Ig receptors or defective Fc-like receptors in cancer cells, because the specification does not provide evidence that said defective receptors exist in cancer cells and one of skill in the art would not know in which cancer cells to find said defective receptors.

7. Claims 7, 12, in part, 13-15, 17 in part, 18 in part, 19, 69, 71 and 92 are drawn to methods of detecting loss of immunoglobulin regulation of steroid hormone responsive cell growth.

The specification has identified the poly-Ig receptor as the epithelial receptor for IgA and IgM (example 24) and an "Fc-like" epithelial receptor for IgG1 (example 25). The specification has not provided any identity of mutated or otherwise defective poly-Ig receptors or Fc-like receptors. The specification has demonstrated that IgA, IgM or IgG1 can inhibit the growth of steroid dependent cancer cell lines in culture. The specification has not provided any evidence that this phenomenon would not be applicable to normal non-cancerous cells, or that cancer cells in culture or in vivo have defective poly-Ig receptors or Fc-like receptors which cannot mediate the observed inhibition. It is noted that all the cancer cells set forth in specific examples by the specification are inhibited by the immunoglobulins and therefore exhibit functional inhibition of steroid hormone responsive cell growth and therefore would not be expected to have defective or decreased poly-Ig or defective or decreased Fc-like receptors. Therefore one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to carry out the claimed methods with respect to the identification of defective poly-Ig receptors or defective Fc-like receptors in cancer cells, because the specification does not provide evidence that said defective receptors exist in cancer cells. It appears from the evidence presented in the specification, that the cancer cell lines tested are under the control of the receptor which responds to the serum inhibitors. The specification does not provide any objective evidence that cancer cells in vivo are not able to respond to said serum inhibitors, therefore there would be no reasonable expectation of success to screen for defective poly-Ig of defective Fc receptors in cancer cells.

8. Claims 8, 67 and 91 are rejected under 35 U.S.C. 102(b) as being anticipated by Harris et al (Am J Pathol, 1981, Vol. 105, pp. 47-53) as evidenced by Cargo et al (Journal of Experimental Medicine, 1978, pp. 1832-1836).

Claim 8 is drawn to a method of detecting a mediator of immunoglobulin inhibition of steroid hormone responsive cell growth wherein said inhibition can be reversed by steroid hormone, the method comprising detecting in a mucosal epithelial cell a receptor capable of

binding the Fc domain of a dimeric/polymeric IgA or polymeric IgM, wherein a detected receptor is capable of binding the Fc domain of dimeric/polymeric IgA or polymeric IgM is indicative that said receptor is a mediator of immunoglobulin inhibition of steroid hormone responsive cell growth wherein the inhibition is capable of being reversed by said steroid hormone.

Claims 67 and 91 embody the method of claim 8 wherein the poly-Ig receptor is detected.

Harris et al disclose a method for detecting Secretory Component in breast ductal epithelial cells (page 49, Table 1), and breast and ovarian carcinomas (page 50, Table 2). Cargo et al provides evidence that secretory component on epithelial cells is the same as the poly-Ig receptor (page 1832, Title). The property of modulating the inhibition of steroid hormone responsive cell growth would be inherent in the secretory component on the breast cells.

9. Applicant has provided extensive arguments regarding the adequate written description of the estrogen binding "activity" citing the specification which describes the function of said "activity" . However, there is not support in the specification that about the molecular weight of the activity, or a partial amino acid sequence of said activity. Further, there is no positive evidence that the estrogen binding activity is an estrogen receptor, having all of the activities of an estrogen receptor, such as translocating to the nucleus when bound by estrogen..

10. All other rejections and objections as set forth in the previous Office action are withdrawn in light of applicants amendment and arguments.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
5/2/2005